

Application No. 09/830,191
RCE/Amendment Dated Dec. 4, 2003
Reply to Final Office Action of June 4, 2003

REMARKS/ARGUMENTS

By this Amendment, Claims 13, 15, 19 and 22 are canceled, Claims 10, 11, 16, 17, 18 and 20 are amended. Claims 10-12, 14, 16-18 and 20-21 are pending.

Claim 10 has been amended to specify more precisely the scope of the invention.

In particular,

- the definition of the coating of the ibuprofen granules has been limited to mixture consisting in components (A) to (D) in specific amounts;
- the nature of component (D), as it appeared in former claim 15, has been included;
- the dissolution time of the coated granules has been specified (according to former claim 13) and page 6, lines 19-23.

Corresponding limitations have been introduced in process claim 17, which has further been limited to the successive steps (and not simultaneous) of granulating and coating.

Claims 10-22 are rejected under 35 USC 103(a) as being unpatentable over Carli et al. (US 5,275,824) and Dunn et al. (US 4,308,251) in view of Ghanta et al. (US 5,814,332).

Applicants respectfully traverse this ground of objection for the following reasons.

The invention is intended to provide for coated granules of ibuprofen which present a good bioavailability, a taste masking and a non irritant effect on the throat. This is obtained due to the specific composition according to the invention in which, the coated ibuprofen particles based on granulated ibuprofen microcrystals are coated by a coating composition consisting of a mixture consisting in

- A) 5 to 50% by weight of ethyl cellulose, based on the ibuprofen,
- B) 10 to 60% by weight, of hydroxypropyl methyl cellulose (HPMC), based on the ethyl cellulose,

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- C) 0.1 to 40% by weight, of silica with antistatic and permeabilizing properties, based on the ethyl cellulose, and
D) 0 to 50% by weight of an agent favoring the solubilization of the ibuprofen, based on ibuprofen, at least one of said constituents (A)-(D) can be used for the granulation of the ibuprofen microcrystals.

This specific composition is not described nor suggested by the cited references, either taken alone or together.

As a matter of fact, as explained below, two of the cited references (Carli et al and Dun et al) teach sustained-release formulations and are silent on the taste-masking properties and the other one (Ghanta et al) describes a completely different structure, in which the function of each constituent is well defined.

Carli et al. describes therapeutic compositions with controlled release of medicaments. In particular, it describes medicament-loaded particles coated with polymer delay films. The coating polymer can be ethyl cellulose, as in examples 9-11. However, in said examples, in the one hand, the coating never contains colloidal silica (which is one component of the granulated medicament) and ethyl cellulose is used in very large amount of at least 80% by weight on the basis of the active substance, and in the other hand, the dissolution time of the active substance in a buffer of pH7.5 after 30 min is only 13% for example 10 and 49% for example 11 (see Table 3), whereas it is of 80% in the case of the coated granules according to the invention.

Dun et al. describes delayed-disintegration tablets of a therapeutic agent which can be ibuprofen, which allow a prolonged dissolution time of the therapeutic agent. Said tablets are prepared by wet granulating the therapeutic agent with an erosion-promoting agent and a release-controlling agent, which can be ethyl cellulose or HPMC, drying the granular wet mass, reducing to the desired size and then tableting, as explained at column 4 lines 1-5 and column 5 lines 52-67. In no way there is formation of a coating layer on the surface of the therapeutic agent

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granules.

Ghanta et al. describes taste-masked microcapsules of water-insoluble NSAID drug, like ibuprofen, useful for preparing chewable tablets, in which cellulose acetate phthalate and gelatin are the microencapsulating polymer microcapsule wall materials. Due to said specific dual coating, a high bioavailability of the ibuprofen core is provided to (thanks to the gelatin part) as well as a taste masking effect (thanks to the cellulose acetate phthalate).

There is no incitation to combine the teachings of either Carli et al. or Dun et al. with the teaching of Ghanta et al. since the first ones relate to sustained release preparations while the other one relates to rapid release preparation.

Thus, even if those references are combined, the person skilled in the art could not deduce the present invention.

In fact, there is no incitation in Dun et al. or Carli et al. to substitute gelatin of Ghanta et al. for another agent which could confer taste masking effect.

Claims 10-22 are thus inventive over Carli et al. and Dunn et al. in view of Ghanta et al..

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

Should the Examiner believe that anything further is desirable in order to place the

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application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

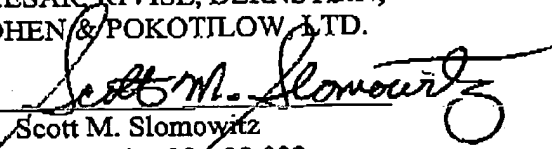
December 4, 2003

Please charge or credit our
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Respectfully submitted,

CAESAR, RIVISE, BERNSTEIN,
COHEN & POKOTILOV, LTD.

By


Scott M. Slomowitz
Registration No. 39,032
Customer No. 03000
(215) 567-2010
Attorneys for Applicants